

### **Abstract of the Disclosure**

The disclosure describes a method for isolating genes encoding proteins that regulate the expression of target genes of interest, said method designated herein for convenience by the term: "Cre-Trap cloning." In brief, the Cre-trap cloning method of the invention involves modifying a target gene of interest such that it encodes the Cre recombinase and Herpes simplex virus (HSV) thymidine kinase (TK) proteins. This step is followed by mutagenesis and selection for cells which have lost target gene expression by virtue of their resistance to ganciclovir (a nucleoside analog structurally related to acyclovir), which kills cells expressing HSV TK. Cell lines that have lost target gene expression due to mutations in genes encoding *trans*-acting factors are then transiently transfected with a cDNA library from the parent cell line in a novel expression vector (pCT.1, shown in Figure 1). Expression of a cDNA that complements the genetic mutation results in expression of the target gene and production of the Cre recombinase, which modifies pCT.1 in such a way that it is readily isolated from pCT.1 plasmids with cDNAs that do not activate target gene expression.